Claims

1. A soluble, fused MHC heterodimer:peptide complex comprising:

a first DNA segment encoding at least a portion of a first domain of a selected MHC molecule;

a second DNA segment encoding at least a portion of a second domain of the selected MHC molecule;

a first linker DNA segment encoding about 5 to about 25 amino acids and connecting in-frame the first and second DNA segments;

wherein linkage of the first DNA segment to the second DNA segment by the first linker DNA segment results in a fused first DNA-first linker-second DNA polysegment;

a third DNA segment encoding an antigenic peptide capable of associating with a peptide binding groove of the selected MHC molecule;

a second linker DNA segment encoding about 5 to about 25 amino acids and connecting in-frame the third DNA segment to the fused first DNA-first linker-second DNA polysegment;

wherein linkage of the third DNA segment to the fused first-first linker-second DNA polysegment by the second linker DNA segment results in a soluble, fused MHC heterodimer:peptide complex.

2. The soluble, fused MHC heterodimer:peptide complex of claim 1, wherein the selected MHC molecule is an MHC Class II molecule.

3. The soluble, fused MHC heterodimer:peptide complex of claim 2, wherein the first DNA segment encodes a $\beta 1$ domain.

4. The soluble, fused MHC heterodimer:peptide complex of claim 2, wherein the second DNA segment encodes an $\alpha 1$ domain or $\alpha 1 \alpha 2$ domains.

5. The soluble, fused MHC heterodimer:peptide complex of claim 1, wherein the selected MHC molecule is selected from the group consisting of IA^{g7}, IA^{s}, DR1β*1501 and DRA*0101.

6. The soluble, fused MHC heterodimer:peptide complex of claim 1, wherein the selected MHC molecule is an MHC Class I molecule.

7. The soluble, fused MHC heterodimer:peptide complex of claim 1, wherein the first linker DNA segment is GASAG (SEQ. ID. NO. 29) or GGGGSGGGGSGGGGS (SEQ. ID. NO. 36).

8. The soluble, fused MHC heterodimer:peptide complex of claim 1, wherein the second linker DNA segment is GGSGG (SEQ. ID. NO. 30) or GGGSGGS (SEQ. ID. NO. 31).

9. The soluble, fused MHC heterodimer:peptide complex of claim 1, wherein the third DNA segment encodes an antigenic peptide capable of stimulating an MHC-mediated immune response.

10. The antigenic peptide of claim 9, wherein the peptide is selected from the group consisting of a mammalian GAD 65 peptide, (SEQ ID NO: 59), (SEQ. ID. NO. 61), (SEQ ID NO:40), (SEQ. ID. NO. 39) and a mammalian mylein basic peptide(SEQ. ID. NO. 33).

11. The soluble, fused MHC heterodimer:peptide complex of claim 1, wherein said MHC heterodimer:peptide complex further comprises a fourth DNA segment encoding at least a portion of a third domain of the selected MHC molecule, and a third linker DNA segment encoding about 5 to about 25 amino acids and connecting in-frame the second and fourth DNA segments resulting in a fused third DNA-second linker-first DNA-first linker-second DNA-third linker-fourth DNA polysegment.

12. The soluble, fused MHC heterodimer:peptide complex of claim 11, wherein the selected MHC molecule is an MHC Class I molecule.

13. The soluble, fused MHC heterodimer:peptide complex of claim 11, wherein the selected MHC molecule is an MHC Class II molecule.

14. The soluble, fused MHC heterodimer:peptide complex of claim 11, wherein the fourth DNA segment is a β2 chain.

15. The soluble, fused MHC heterodimer:peptide complex of claim 11, wherein the third linker DNA segment is GGGGSGGGGSGGGGSGGGGSGGGGS (SEQ. ID. NO. 32).

16. An isolated polynucleotide molecule encoding a soluble, fused MHC heterodimer:peptide complex of claim 1.

17. A fusion protein expression vector capable of expressing a soluble, fused MHC heterodimer:peptide complex of claim 1, comprising the following operably linked elements:

a transcription promoter;

a first DNA segment encoding at least a portion of a first domain of a selected MHC molecule;

a second DNA segment encoding at least a portion of a second domain of the selected MHC molecule;

a first linker DNA segment encoding about 5 to about 25 amino acids and connecting in-frame the first and second DNA segments;

wherein linkage of the first DNA segment to the second DNA segment by the first linker DNA segment results in a fused first DNA-first linker-second DNA polysegment;

a third DNA segment encoding an antigenic peptide capable of associating with a peptide binding groove of the selected MHC molecule;

a second linker DNA segment encoding about 5 to about 25 amino acids and connecting in-frame the third DNA segment to the fused first DNA-first linker-second DNA polysegment;

wherein linkage of the third DNA segment to the fused first DNA-first linker-second DNA polysegment by the second linker DNA segment results in expression of a soluble, fused MHC heterodimer:peptide complex; and

a transcription terminator.

18. The expression vector of claim 17, wherein said MHC heterodimer:peptide complex further comprises a fourth DNA segment encoding at least a portion of a third domain of the selected MHC molecule, and a third linker DNA segment encoding about 5 to about 25 amino acids and connecting in-frame the second and fourth DNA segments resulting in a fused third DNA-second linker-first DNA-first linker-second DNA-third linker-fourth DNA polysegment.

19. A soluble, fused MHC heterodimer:peptide complex produced by culturing a cell into which has been introduced an expression vector according to claim 17, whereby said cell expresses a soluble, fused MHC heterodimer:peptide complex encoded by the DNA polysegment; and recovering the soluble, fused MHC heterodimer:peptide complex.

20. A pharmaceutical composition comprising a soluble, fused MHC heterodimer:peptide complex of claim 1 in combination with a pharmaceutically acceptable vehicle.

21. An antibody that binds to an epitope of a soluble, fused MHC heterodimer:peptide complex of claim 1.

22. A method of treating a patient to decrease an autoimmune response, the method comprising inducing immunological tolerance in said patient by administering a

therapeutically effective amount of a soluble, fused MHC heterodimer:peptide complex of claim 1.

23. A method for preparing a responder cell clone that proliferates when combined with a selected antigenic peptide presented by a stimulator cell, comprising:

isolating non-adherent, CD56-, CD8- cells that are reactive with the selected antigenic peptide, thereby forming responder cells;

stimulating the responder cells with pulsed or primed stimulator cells;

restimulating the stimulated responder cells with pulsed or primed stimulator cells; and

isolating a responder cell clone.

24. The method of claim 23, wherein the responder cells are isolated from a prediabetic or new onset diabetic patient.

25. The method of claim 23, wherein the responder cell clone is a T cell clone.

26. The method of claim 23, wherein the selected antigenic peptide is a GAD peptide.

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